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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,625	08/25/2003	Eva Vranova	2676-6062US	3614

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/647,625	VRANOVA ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11 and 14-23* is/are pending in the application.

4a) Of the above claim(s) *1-5,11,14-17,19,20,22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,9,10,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/25/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 7/31/2006, in which claims 8 and 12-13 were canceled; and claims 11, 18 and 21 were amended. Currently, claims 1-7, 9-11 and 14-23 are pending.

Election/Restrictions

Applicant's election without traverse of Group I and SEQ ID NOS: 168 and 169 in the reply filed on 7/31/2006 is acknowledged. The response states, "To the extent the sequence election is understood, applicants would like to elect a nucleic acid sequence that encodes the peptide of SEQ ID NO: 169 (e.g., SEQ ID NO: 168). If that is appropriate, applicant's election is without traverse." The election of both sequences is appropriate.

Claims 1-5, 11, 14-17, 19-20 and 22-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/31/2006.

An examination on the merits of claims 6-7, 9-10, 18 and 21 follows.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office on 2/23/2001. It is noted, however, that applicant has not filed a certified copy of the 01200659 9 application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

Receipt of an unsigned information disclosure statement (IDS), filed on 8/25/2003 is acknowledged. A signed information disclosure statement for previously submitted references was filed on 7/31/2006. The references have been considered. The signed and initialed PTO 1449, filed 8/25/2003, has been mailed with this action.

Specification

The disclosure is objected to because of the following informalities: two different clones are labeled as SEQ ID NO: 161 in Table 1 (page 24, clones t7-2-4.seq and t7-4-7.seq). Table 2 identifies all genes that were confirmed as upregulated by Northern blot. Thus, it appears as though clone t7-2-4.seq should have been labeled as SEQ ID NO: 160.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7, 9, 10, 18 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is vague and indefinite in that the metes and bounds of the term "polypeptide sequence" are unclear. It is unclear if the term is referring to an actual polypeptide molecule or a

written polypeptide sequence. It would be remedial to amend the claim to delete the word sequence to clearly indicate that the polypeptide molecule is being claimed.

Claim 7 is vague and indefinite in that the metes and bounds of the phrase "isolating said differentially expressed sequence" are unclear. It is unclear if the phrase is referring to a written sequence or the sequence of a molecule, such as a nucleic acid molecule. It would be remedial to amend the claim to replace the references to a "sequence" with the term "nucleic acid."

Claims 9, 10, 18 and 21 depend from claim 7 and are indefinite for the same reasons as applied to claim 7. It would be remedial to amend these claims to replace the term "sequence" with the term "nucleic acid" such that claim 7 provides proper antecedent basis for the term.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 18 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a set of differentially expressed sequences that are either up- or down-regulated between plants that are stress-adapted and nonadapted after application of a sublethal stress to isolated plant material (i.e. any plant tissue or intact plant). The sequences may be isolated from any plant (for example, tobacco, rice, bell pepper, potato, etc.) of any

species or cultivar. Furthermore, the sequences may be isolated from any type of tissue (for example, leaf, root, etc.). The sublethal stress may be any type of stress including pathogen stress, water stress, or oxidative stress by any number of compounds, for example. Claim 18 is drawn to a promoter sequence of any differentially expressed sequence of claim 7. Accordingly, the claims are drawn to an enormous genus of sequences that have the common property of differential expression but may vary widely in terms of structure.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification envisions the isolation of differentially expressed genes or gene fragments from any plant material by any type of stress (biotic or abiotic) (e.g. paragraphs [0009]-[0011]). The specification envisions using techniques such as differential display, messenger RNA subtraction, filter hybridization or micro-array techniques to identify the differentially expressed transcripts (e.g. paragraph [0012]). The specification teaches the application of methyl viologen (MV) to leaf tissue of *Nicotiana tabacum*, and the identification of approximately 170 partial expressed sequences that are induced or repressed upon stress adaptation by MV (e.g. paragraph [0008], [0036]-[0039] and [0051]; Table 1). Expression of 16 genes was analyzed by Northern analysis with RNA from and independent experiment, and the induction of 12 genes was confirmed (e.g. paragraph [0051]). Thus, four of the sixteen genes were not confirmed. Accordingly, the specification describes twelve sequences that are induced in tobacco leaves upon exposure to MV: SEQ ID NOS: 52, 66, 106, 117, 131, 137, 138, 143,

148, 149, 142 and 160 (e.g. Table 2). SEQ ID NO: 117 is contained within SEQ ID NO: 168, which encodes the protein of SEQ ID NO: 169 (e.g. Table 2, sequence listing). The specification teaches the SEQ ID NO: 152 is known in the art as Accession Number emb|X66942 (e.g. Table 2). The specification teaches the isolation of the full-length cDNA for SEQ ID NO: 117, which is SEQ ID NO: 168 (e.g. Example V). The specification does not describe the full-length cDNA for any other sequence.

With regard to promoter sequences, the specification envisions using methods known in the art to identify the promoter sequences of the differentially expressed sequences (e.g. paragraph [0018]). The specification does not teach the isolation of any promoter sequence for any of the 167 partial cDNA sequences obtained in the MV assay. There is no known or disclosed correlation between the claimed differential expression and the structure of the regulatory elements of those genes that are differentially expressed. Furthermore, there is no disclosure of the promoter sequences.

Even if one accepts that the examples of differentially expressed sequences described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of widely varying species within the claimed genus. The confirmed cDNA sequences of table 2 do not have a common structure related to the differential expression. Based upon the sequence analysis presented in table 2, the proteins are likely to be synthetases, kinases, transcription factors, etc. The results are not necessarily predictive of other structures from tobacco leaves other tissues of tobacco plants or plants other than tobacco. Thus, it is impossible for one to extrapolate from the examples described herein a representative number of species that would fully describe the claimed genus.

The prior art does not provide evidence of any partial structure that would be expected to be common to the members of the genus. The prior art teaches that even within families of related genes, responses to stress may vary. Hiraga et al (FEBS Letters, Vol. 741, pages 245-250, 2000) teach that secretory class III plant peroxidases (POXs) catalyze the oxidation of various reductants (e.g. Abstract). Among 21 POX genes tested, Hiraga et al teach that seven genes responded to external stimuli such as wounding, UV-irradiation and treatments with ethephon, paraquat and MeJA, while the remaining 14 genes did not respond at al (e.g. section 3.2; Table 3). Some genes were preferentially expressed in roots and some genes were preferentially expressed in aerial parts (e.g. section 3.2). Thus, even with genes of the same family, different responses to stress are obtained. Furthermore, the prior art teaches that different cultivars can have different responses to stresses. Martinez et al (Plant Science, Vol. 160, pages 505-515, February 5, 2001) teach that *Solanum curtilobum* has markedly increased activities of FeSOD and Cu/ZnSOD with increasing level of PEG-induced water stress or MV-mediated oxidative stress, whereas *Solanum tuberosum* has unaltered levels of SOD activities in response to water stress and markedly decreases MnSOD and Cu/ZnSOD activities in response to MV-mediated oxidative stress (e.g. page 512, paragraph bridging columns).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed

chemical structure of the encompassed genus of differentially expressed sequences and promoter sequences thereof, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of differentially expressed sequences and promoters thereof encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to a common structure within the genus, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision a representative number of differentially expressed sequences and promoters that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 7, 18 and 21.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al (The Plant Journal, Vol. 14, No. 3, pages 317-326, 1998; see the entire reference).

Regarding claim 7, Chen et al teach the isolated fibrillin transcript, which is differentially expressed in leaves of wounded or drought-stressed bell pepper plants (e.g. Figure 5). Chen et al teach that fibrillin expression is increased in stress-adapted plants in response to a variety of stresses, including drought, wounding, and paraquat (methyl viologen) exposure (e.g. pages 322-323, Accumulation of fibrillin in bell pepper leaves under drought or mechanical wounding stress; page 323, Superoxide involvement in the regulation of fib expression and the effect of paraquat).

Regarding claim 18, Chen et al teach the construction of fibrillin promoter expression fusions (e.g. page 324, Construction of promoter expression fusions).

Claims 7 and 18 read on the teachings of Chen et al, because Chen et al teach that the fibrillin gene is expressed in the leaves of stress-adapted plants and is expressed in nonadapted plants at a low or undetectable level (e.g. paragraph bridging pages 318-319). Thus, if one were to perform a method of isolating bell pepper leaf material, inducing stress adaptation (e.g. by paraquat as taught by Chen et al), identifying differential expression of a sequence, and isolating

the differentially expressed sequence, one would isolate the fibrillin gene taught by Chen et al. Thus, Chen et al teach a species that anticipates the claimed genus of sequences of interest.

Claims 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Deruere et al (The Plant Cell, Vol. 6, pages 119-133, 1994; see the entire reference), as evidenced by Chen et al (The Plant Journal, Vol. 14, No. 3, pages 317-326, 1998; see the entire reference).

Regarding claim 7, Deruere et al teach the nucleic acid sequence of the bell pepper fibrillin cDNA (e.g. paragraph bridging pages 125-126; Figure 6A).

Regarding claim 21, Deruere et al teach the nucleic acid sequence of the fibrillin cDNA in an expression vector (e.g. paragraph bridging pages 125-126).

The Chen et al reference is cited only to show that the bell pepper fibrillin cDNA is differentially expressed. Chen et al teach that the fibrillin gene is expressed in the leaves of stress-adapted plants and is expressed in nonadapted plants at a low or undetectable level (e.g. pages 322-323, Accumulation of fibrillin in bell pepper leaves under drought or mechanical wounding stress; page 323, Superoxide involvement in the regulation of fib expression and the effect of paraquat; paragraph bridging pages 318-319). Thus, if one were to perform a method of isolating bell pepper leaf material, inducing stress adaptation (e.g. by paraquat as taught by Chen et al), identifying differential expression of a sequence, and isolating the differentially expressed sequence, one would isolate the fibrillin gene taught by Deruere et al. Thus, Deruere et al teach a species that anticipates the claimed genus of sequences of interest.

Claims 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hiraga et al (FEBS Letters, Vol. 471, pages 245-250, 2000; see the entire reference).

Regarding claim 7, Hiraga et al teach rice EST clones prxRPA, R2576, R2184, R2693, C52903, R2329 and S11222, which are induced differentially by external stimuli, including paraquat, in the leaf blades of 16-day-old plants (e.g. page 249, left column; Figure 2).

Regarding claim 21, the EST sequences are clones and thus are contained within a vector (e.g. Table 1).

Claims 7 and 21 read on the teachings of Hiraga et al, because Hiraga et al teach that the expression of the abovementioned ESTs is induced in response to a variety of stress stimuli, and thus are differentially expressed between stress adapted and nonadapted rice plants (e.g. Figure 2). Hiraga et al teach that the EST expression is increased after isolating plant leaf material, inducing stress adaptation (e.g. by incubating with a solution containing paraquat) (e.g. page 245, section 2.2; Figure 2). Thus, if one were to isolate rice plant leaf material, induce stress adaptation in the isolated plant material by application of a sublethal stress, identify differential expression of a sequence between stress-adapted and nonadapted plant material, and isolate differentially expressed sequences, one would isolate the EST sequences taught by Hiraga et al. Accordingly, Hiraga et al teach multiple species that anticipate the claimed genus of sequences of interest.

Claims 7 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen and Chen (Plant Molecular Biology, Vol. 42, pages 387-396, 2000; see the entire reference).

Regarding claim 7, Chen and Chen teach the identification of tWRKY3 and tWRKY4 from tobacco (e.g. page 390, Identification of tWRKY3 and tWRKY4; Figure 1). Chen and Chen teach the induction of both genes by TMV-infection (pathogen stress) and salicylic acid (SA) treatment (e.g. page 392, Induction of tWRKY3 and tWRKY4 by TMV infection; page 393, Induction of WRKY3 and tWRKY4 by SA and its structural analogs).

Regarding claim 21, Chen and Chen teach the insertion of the differentially expressed tWRKY3 and tWRKY4 sequences into pCR2.1 vector and pET32b vector (e.g. page 389, Domain-specific differential display, Expression and purification of WRKY protein in Escherichia coli).

Claims 7 and 21 read on the teachings of Chen and Chen, because Chen and Chen teach that the expression of the abovementioned WRKY genes is induced in response to a variety of stress stimuli. The sequence taught by Chen and Chen would be identified by the assay of claim 7. Therefore, Chen and Chen teach two species that anticipate the claimed genus of sequences of interest.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession No. X66942 (GI: 19969, December 8, 1992; see the entire reference).

GenBank Accession No. X66942 teaches the nucleic acid and amino acid sequence of *N. tabacum* prb-1b gene.

Claim 7 reads on the teachings of GenBank Accession No. X66942, because the specification teaches that this sequence is induced upon stress adaptation (e.g. Table 2). Thus, the sequence taught in the accession number inherently possesses the claimed characteristics of

being able to be isolated by isolating plant material, inducing stress adaptation in said isolated plant material by application of a sublethal stress, identifying differential expression of a sequence between stress-adapted and nonadapted plant material, and isolating said differentially expressed sequence. Accordingly, the sequences disclosed in GenBank Accession No. X66942 meet each of the limitations of the rejected claim.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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